The Mystery of Ontario’s Unusually High Pancreatic Cancer Survival

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Outline

• The mystery & the clues
• The suspect & the evidence
• A possible solution
• Conclusions and further sleuthing
The mystery

• C-SPAN (Cancer survival & prevalence analytic network) calculated survival for major cancers using the CCR:
  • Ages 15-44, 45-54, 55-65, 65-74, 75-99
  • Province, Sex (where possible)
  • 1, 3, 5, & 10 year relative survival
The mystery

• For most estimates, Ontario’s survival were similar to those from other provinces

• For pancreatic cancer, Ontario’s survival was unusually high
  • 2004-07, 5-year age-standardized period relative survival estimate: Ontario, 10.2; other provinces, 3.4 to 5.9
The clues

• Age group, diagnosis period and time since diagnosis were examined to determine, if possible, how Ontario’s survival differs from the other provinces.

• Ontario’s survival was different for:
  • 15-44, 1-year, all periods
  • 65-74 & 75-99, 3- & 5-year, all periods
  • 2001-3 & 2004-7 periods, 3-year, all ages
Data quality suspect #1

• Incorrect inclusion/exclusion of cases
  • If residence is missing, include
  • ON’s conservative multiple primary rules
  • Too many surgery without pathology cases; maybe not really cancer?
  • Autopsy only and death certificate only cases routinely excluded from survival analyses
Data quality suspect #2

- Bias in determination of diagnosis date
  - Hall et al, 2006, compared head and neck cases from the OCR to a clinical series and found that diagnosis dates in the OCR were significantly earlier
  - This can also occur when two primaries are resolved as one.
Data quality suspect #3

• Bias in determination of vital status
  • National death clearance does not include Quebec
  • Can not use the provincial health insurance file to censor those who emigrate from the province
These issues overlap!

- Example: Death certificate only
  - Incident case may have been diagnosed elsewhere
  - No match to case due to linkage failure
  - Date of diagnosis unknown, but survival tends to be short
  - Cause of death may be inaccurate (Hall et al, cause of death had 31% error rate)
Follow the Evidence!
The culprit: lost to follow-up

- Ontario uses only passive registration methods
  - Relies on linkages to mortality data or reports from treatment clinics and hospitals for vital status and date of death
- Usual assumption: cases lost to follow-up are alive at the end of the study
Ontario pancreas data

• 12,379 cases diagnosed 1992-2003
• Followed to December 31, 2008
• Excludes
  • 700 DCO cases (5.3%)
  • 7 Autopsy only cases
  • 26 cases with missing residence
Sample survival data

- Finnish colon cases (Dickman & Lambert)

\[ \text{%Lost} = \frac{8}{35} = 22.9\% \]
\[ \text{%Alive} = \frac{10}{27} = 37.0\% \]
Follow-up & survival: sex

Percent

%Lost

Female: 3.0
Male: 2.3

%Alive

Female: 1.4
Male: 1.4
Microscopic confirmation

Percent

%Lost

No
15

%Alive

No
1.0

Yes
1.9

1.9

0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0

No

Yes
Surgery

Percent

%Lost

- No: 2.3%
- Yes: 5.8%

%Alive

- No: 7.7%
- Yes: 0.8%
Diagnosis period

Percent

%Lost

1992-94: 1.9
1995-97: 2.9
1998-00: 2.2
2001-03: 3.5

%Alive

1992-94: 1.0
1995-97: 1.2
1998-00: 1.6
2001-03: 1.8
Beale code

Percent

- Large Metro
- Large Metro Fringe
- Medium Metro
- Small Metro
- Non-metro Adjacent
- Non-metro non-adjacent

%Lost

3.3 3.3 2.2 2.0 2.5 1.7

%Alive

1.4 2.3 1.3 1.2 1.0 1.1
Age group

Percent

%Lost

15-44
45-54
55-64
65-74
75-99

%Alive

15.1
3.0
2.0
1.2
0.2

19
Median observed time

Months

Lost

Died

- 15-44
- 45-54
- 55-64
- 65-75
- 75-99

- 1.1
- 0.9
- 1.3
- 0.4
- 0.6
- 0.9
- 1.3
- 0.4
- 0.6

- 6.4
- 5.2
- 4.4
- 3.3
- 2.0
Paper #1

- Brenner & Hakulinen (2009)
- Finnish Cancer Registry, 20 common cancers, dx 1985-9, follow-up 2004
- Under-ascertainment of deaths:
  - Imperfect death linkage, 0.1-5%
  - Unregistered emigration, 0.05-2%
Paper #1 Results

• “Even modest levels of under-registration of deaths may lead to severe overestimation of long-term survival estimates”

• Worse for
  • Relative survival
  • Older ages
  • Unrecorded emigration
Paper #2

• Johnson, Weir, Yin & Niu (2010)
• SEER data, SEER site recode, dx 1995-2000, follow-up 2005
• Characteristics of synthetic datasets:
  • Incomplete death ascertainment: 2%-10%
  • Follow-up of live patients: none, or incomplete (5%-30%)
Paper #2 Results

• When death ascertainment is complete
  • Minor differences with no follow-up
  • As loss increases, survival estimates decrease
  • Impact greatest for cancers with very high or very low case fatality rates
Paper #2 Results

• When death ascertainment is *incomplete*
  
  • Missing even a small proportion of deaths resulted in high survival
  
  • Impact of missing deaths most evident for cancers with high fatality rates
What’s up with ON?

• Large, growing immigrant population
  • Return to homeland after diagnosis?
• No alternate sources for residence/vital status verification
• Incomplete national death clearance
Loss-adjusted survival

- “Cancer survival in Africa, Asia, the Caribbean and Central America”, IARC 2011. (Chapter 2, Ganesh et al)

- Estimated by assuming that survival of patients lost to follow-up is the same as that for patients with known follow-up and similar prognostic factors.
Observed 5-year survival:

- Assume alive @ 5 years
- Loss-adjusted
- Censor at last contact

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Assume alive</th>
<th>Loss-adjusted</th>
<th>Censor</th>
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<tbody>
<tr>
<td>15-44</td>
<td>23.0</td>
<td>11.7</td>
<td>10.4</td>
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<tr>
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<td>3.6</td>
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<tr>
<td>75-99</td>
<td>2.9</td>
<td>2.0</td>
<td>1.8</td>
</tr>
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</table>
Conclusions

• The assumption that cases lost to follow-up are alive at the cut-off date appears to be responsible for the bias in Ontario’s high pancreatic cancer survival

• The impact of emigration may be greater than expected elsewhere

• Additional linkages should be considered to improve follow-up
Next steps

• Loss correction:
  • Adjust for multiple prognostic factors
  • Explore relative survival and period method
  • Analyze other cancers, especially lung, liver and melanoma

• Further explore the DCOs
References


